Adverse drug events are one of the most common types of harmful errors in both hospitalized and ambulatory patients. Studies have shown that preventable adverse drug events occur in 7 to 10 of every 100 hospital admissions,\textsuperscript{1-3} and may even occur more frequently in the ambulatory setting.\textsuperscript{4} Prescribing errors are likely responsible for at least half of these events.\textsuperscript{5,6}

What Are Computerized Provider Order Entry With Clinical Decision Support Systems?

Computerized provider order entry (CPOE) refers to any system in which clinicians directly enter orders for medications, tests, or procedures into an electronic system, which then transmits the order directly to the recipient responsible for carrying out the order (e.g., the pharmacy, laboratory, or radiology department). These systems were initially implemented in the inpatient setting as a strategy to reduce medication errors, and their use is increasingly being broadened to include entry of all types of orders in both the inpatient and outpatient settings. A CPOE system, at a minimum, ensures standardized, legible, and complete orders and thus has the potential to greatly reduce errors at the prescribing and transcribing stages.

How Have Computerized Provider Order Entry With Clinical Decision Support Systems Been Implemented?

Clinical decision support systems (CDSS) are often integrated with CPOE systems. CDSS provide clinicians with reminders or recommendations in order to optimize the safety and quality of clinical decisions. For example, a medication CDSS may offer default values for doses, routes of administration, and frequency for commonly used drugs. Such systems may also offer more sophisticated drug safety features such as checking for drug allergies or drug-drug interactions, providing reminders for appropriate laboratory monitoring (e.g., reminders to check coagulation parameters if a patient is prescribed warfarin), or even suggesting appropriate orders based on patient-specific factors (e.g., reminders to order prophylaxis against deep venous thrombosis in a patient admitted with a hip fracture).

At the highest level of sophistication, the combination of CPOE and CDSS can therefore prevent errors of commission and errors of omission. Optimal use of CPOE with CDSS in this fashion requires integration across multiple hospital and ambulatory information systems, including the medical record, clinical laboratory, radiology, and pharmacy.

Despite recommendations from a broad range of governmental and non-governmental organizations, the pace of uptake of CPOE and CDSS has remained slow in both the inpatient and outpatient environments.\textsuperscript{7,8} The use of CPOE and CDSS will likely increase with the implementation of the Health Information Technology for Economic and Clinical Health (HITECH) Act, part of the American Recovery and Reinvestment Act of 2009 (ARRA). HITECH stipulates that health care providers must demonstrate the “meaningful use” of
electronic health records (EHR) by 2015, and will include penalties for failing to achieve that standard by 2016. The “meaningful use” criteria requires in part that EHRs must include one clinical decision support rule applied to a specialty or high-priority condition, as well as the ability to track compliance with that rule.

Given that only CPOE systems with an integrated CDSS meet the HITECH criteria for meaningful use, this brief update review will assess the state of the evidence regarding the effectiveness, cost, and implementation issues related to CPOE systems with CDSS capabilities (CPOE+CDSS).

The 2001 “Making Health Care Safer” report reviewed evidence on the effectiveness of CPOE+CDSS, as well as isolated CDSS, at improving medication safety. The review defined level 1 outcomes as adverse drug events (ADEs), and level 2 and 3 outcomes as medication errors and change in prescribing practices, respectively. These definitions were used in order to distinguish the effects of CPOE and CDSS on clinical outcomes (e.g., preventable ADEs) and surrogate outcomes that may not have caused patient harm (e.g., medication errors).

The 2001 review included four studies of CPOE+CDSS, three of which were conducted at the same academic medical center. These studies all found improvement in level 2 and 3 outcomes, but did not document a reduction in preventable ADEs. All of the studies included in the report evaluated “homegrown,” institution-specific systems (as opposed to commercial system purchased from vendors) and often focused on safety of a specific medication or medication class (such as antibiotics). These factors limit the generalizability of these studies to general ADE prevention and to other institutions. The review also noted the high cost and complex implementation issues that accompany CPOE+CDSS, stating, “CPOE requires a very large up-front investment with more remote, albeit substantial returns. In addition, CPOE affects clinicians and workflow substantially. Its complexity requires close integration with multiple systems, such as the laboratory and pharmacy systems. Failure to attend to the impact of such a large-scale effort on organizational culture and dynamics may result in implementation failure (page 71).”

The overall conclusion of the review was that CPOE+CDSS can lower the rates of medication errors and can promote appropriate prescribing, but evidence of its impact on actual patient-level harm was limited. This conclusion proved to be somewhat controversial. In response, followup commentaries took issue with the fact that CPOE+CDSS received only a “medium strength of evidence” recommendation in the report. The objection to this conclusion centered around the argument that CPOE+CDSS are difficult and costly to evaluate in controlled trials, particularly when evaluating a relatively infrequent single adverse event such as an ADE, and that the face validity of such systems indicated that proof of clinical benefit should not be required before wider adoption. The evidence report’s authors responded that using evidence to evaluate the effectiveness and generalizability of these patient safety practices was essential to their appropriate prioritization and application.
What Have We Learned About Computerized Provider Order Entry and Clinical Decision Support Systems Since the “Making Health Care Safer Report?”

Evidence for the Effectiveness of Computerized Provider Order Entry With Clinical Decision Support Systems

Three systematic reviews published since 2008 have evaluated the effectiveness of CPOE+CDSS at preventing ADEs. Wolfstadt and colleagues\textsuperscript{12} identified ten trials of CPOE+CDSS, nine of which were conducted in the inpatient setting and one in the ambulatory setting. The majority of these studies evaluated homegrown systems, and none were randomized controlled trials. The review concluded that CPOE+CDSS are effective at reducing ADEs, with five of the ten studies finding a statistically significant reduction in ADEs and four others reporting a nonsignificant improvement.

Schedlbauer and colleagues\textsuperscript{13} identified 20 studies that evaluated a total of 27 forms of electronic reminders and prompts embedded in CPOE systems. Only four of these studies were randomized controlled trials (RCTs). The authors classified the alerts as “basic” (including only information about allergies, drug-drug interactions, and default dosing), “advanced” (including alerts targeting errors of omission and patient-specific dosing and safety guidelines), and “complex” (including features of both basic and advanced systems). This review also found that CPOE+CDSS are effective, with 23 of the 27 reminder types demonstrating improvement in targeted outcomes. However, only four of these studies evaluated clinical adverse drug events; three of them did find statistically significant reductions in preventable ADEs. Although the four studies of “complex” alert systems all found significantly improved prescribing practices, only one of these studies found a statistically significant improvement in preventable ADEs.

Van Rosse and colleagues’ review\textsuperscript{14} specifically focused on the effectiveness of CPOE+CDSS in adult and pediatric intensive care units, where patients are particularly vulnerable to ADEs. The 12 observational studies they identified collectively demonstrated reductions in medication prescribing errors; however, no overall effect was found on ADEs or mortality rates.

These three reviews almost exclusively identified studies conducted in the inpatient setting. These studies generally included relatively small patient populations, often within a single hospital or health system, and relatively short intervention periods. The use of CPOE+CDSS in the ambulatory care setting is less extensively studied. Two recent studies\textsuperscript{15,16} conducted in large, community-based practice settings found that mandatory use of CPOE+CDSS achieved reductions in prescribing errors, but not clinical ADEs—mirroring the evidence from the inpatient setting.

Taken together, these reviews indicate that hospitals implementing CPOE+CDSS cannot assume that these systems will reliably reduce clinical ADEs. Insight into the mechanism of this (lack of) effect was provided by a systematic review by Shojania and colleagues\textsuperscript{17} that evaluated the effect of electronic point-of-care reminders on changing physician behavior. This quantitative review found that reminders overall resulted in only small changes in provider behavior, a degree of behavior change that was generally insufficient to yield clinically significant improvement. The authors further concluded that evidence was insufficient to identify key features of systems that could result in clinically significant changes in provider behavior, as the subset of studies reporting the largest effects all originated from a single hospital (Brigham and Women’s...
The conclusions regarding CPOE+CDSS in the 2001 edition of “Making Health Care Safer” thus appear to stand largely unchanged a decade later.

**Computerized Provider Order Entry With Clinical Decision Support Systems Can Affect Workflow and Patient Care Adversely**

The growth in use of CPOE+CDSS has yielded a more nuanced appreciation of the unintended consequences of the technology. These unintended consequences were classified in a seminal 2006 article:18

- More or new work for clinicians
- Unfavorable workflow issues
- Never-ending system demands
- Problems related to persistence of paper orders
- Unfavorable changes in communication patterns and practices
- Negative feelings toward the new technology
- Generation of new types of errors
- Unexpected changes in an institution’s power structure, organizational culture, or professional roles
- Overdependence on the technology

Surveys of clinicians in settings where CPOE was recently implemented have confirmed that clinicians perceive these unintended consequences to be common and to affect patient care adversely.19 An illustration of this phenomenon was provided in a recent study20 that evaluated the effect of a “hard-stop” warning that essentially prevented co-prescribing of the anticoagulant warfarin and the antibiotic trimethoprim-sulfamethoxazole—a combination associated with serious bleeding risks. The warning was abandoned after 6 months because four patients experienced delays in needed treatment with one of the drugs. Another potential effect of these electronic programs is the potential to create more workarounds, or bypassing a recognized problem as a temporary solution, that may then lead to future systems failures.

One particular problem, “alert fatigue,” was discussed in the original “Making Health Care Safer” report and has been further studied over the past decade. Alert fatigue refers to the tendency of clinicians to ignore warnings that are not perceived as being clinically significant, which may result in inappropriately ignoring critical alerts. Alert fatigue is now a well-documented phenomenon in both the inpatient and ambulatory settings,21 as most existing CPOE+CDSS systems lean toward providing comprehensive alerts for all potential drug safety problems rather than focusing alerts on the most clinically significant problems. In one study of an outpatient CPOE+CDSS system,22 more than 300 alerts were required to prevent one ADE, and another study found that clinicians ignored 75 percent of even “critical” drug-drug interaction alerts.23

CPOE+CDSS systems thus have the potential to affect clinician workflow and patient care adversely. These unintended consequences have forced health care systems to pay very close attention to how this technology is configured and implemented.

**Implementation and Costs**

Implementation issues around CPOE+CDSS chiefly involve two aspects: the technical specifications of how the system is configured to minimize alert fatigue and other workflow-
related consequences, and how the transition from paper-based systems to an electronic system is handled.

Some studies have successfully “tailored” alerts by incorporating patient-specific characteristics into algorithms for displaying drug warnings. Seidling and colleagues implemented a tailored alert system at a German hospital and found a reduction in prescribing errors; this study is notable because providers accepted nearly 25 percent of warnings, much higher than rates generally reported in the literature. However, efforts to tailor drug warnings are currently limited by the lack of standardized consensus definitions for drug-drug interactions that are likely to lead to ADEs and unclear malpractice implications for users and manufacturers of CDSS systems should patients be harmed if an alert is not provided. Recent commentaries have called for better guidance and legal protections to allow greater tailoring of alerts to minimize alert fatigue and improve the safety performance of decision support systems, and a recent consensus conference identified the key issues in developing more effective alert mechanisms.

At the institutional level, it is clear that careful attention must be paid to the implementation process of CPOE+CDSS, particularly with regard to how systems are integrated into existing clinician workflow. Unfortunately, no clear consensus exists on the optimal implementation methods in either the hospital or ambulatory setting. The “CDSS five rights” provides a framework on implementation to improve medication management and outcomes by linking each intervention with a specific objective. This framework includes each “right” to be addressed to ensure an optimal CDS program: right information, to the right person, in the right format, through the right channel, at the right point in workflow. The Agency for Healthcare Research and Quality has published the online “Guide to reducing unintended consequences of electronic health records” (www.ucguide.org), and several case studies of implementation of commercial CPOE+CDSS systems have also been published. These reports likely provide the most useful guides for decisionmakers regarding implementation issues.

We did not identify any formal cost-effectiveness analyses of CPOE+CDSS published in the past 5 years. Individual institutions with homegrown CPOE+CDSS systems have estimated considerable cost savings due to ADE prevention and optimizing medication use, but these data may not be generalizable to other settings and systems. A 2009 review of the costs and benefits of health information technology found “a paucity of meaningful data on the cost-benefit calculation of actual IT implementation”, and concluded, “although there is some empirical evidence to support the positive economic value of an EHR system and the component parts of EHRs, projections of large cost savings assume levels of health IT adoption and interoperability that we are nowhere near achieving.”

**Conclusions and Comment**

The 2001 “Making Health Care Safer” report concluded that evidence for the safety benefits of CPOE (with or without CDSS) was only moderate. Unfortunately, a decade of wider CPOE+CDSS implementation and intensive research does not appear to change that conclusion. CPOE+CDSS appear to be effective at reducing medication prescribing errors, but there is no clear evidence that these systems reduce clinical ADEs in either the inpatient or outpatient setting. Reminder systems can stimulate provider behavior change to improve appropriate care, although these benefits may be relatively small.

Significant progress has been made in understanding the unintended consequences and potential for adverse events associated with CPOE+CDSS implementation, but a lack of
consensus exists on implementation processes, especially for health systems implementing commercial applications. Therefore, while the HITECH act and related measures provide health care organizations with considerable incentive to implement health IT, the actual process of implementation may continue to consist of exercises in trial and error, and the return on investment in health IT systems is not predictable. Health information technology certainly has great potential to improve patient safety, but for the specific example of CPOE+CDSS, it appears that potential remains unrealized. A summary table is located below (Table 1).

Table 1, Chapter 41. Summary table

<table>
<thead>
<tr>
<th>Scope of the Problem Targeted by the PSP (Frequency/Severity)</th>
<th>Evidence or Potential for Effectiveness of the PSPs</th>
<th>Estimate of Cost</th>
<th>Implementation Issues How Much do We Know?/How Hard Is it?</th>
</tr>
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<tbody>
<tr>
<td>Common/Moderate</td>
<td>Low-to-moderate</td>
<td>High</td>
<td>Moderate/Difficult</td>
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References


